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Malaria Diagnosed by Autopsy in a Young Traveler Returning From Uganda: Limitations of Surveillance

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Abstract

Fatal infectious disease acquired during international travel is less likely to be captured through existing surveillance when diagnosis is delayed or missed, especially as autopsy rates decline. Death of a young girl owing to malaria demonstrates needs for increased examination of travel-related deaths through postmortem investigation, autopsy, and expanded surveillance.

Malaria, a mosquito-borne parasitic infection, is one of the most common causes of systemic febrile illness in travelers.[1] In the United States, approximately 1,500 cases of malaria are reported to the Centers for Disease Control and Prevention (CDC) each year, virtually all of which are imported from endemic countries via travelers.[2] While surveillance system data have indicated that infectious diseases account for only a small number of travel-related American deaths,[3,4] ill recent travelers who are not diagnosed will not be identified as having an infectious disease-related illness. This is of particular concern for illnesses that result in death in an era when autopsies are becoming uncommon.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Declaration of Interests

The authors state that they have no conflicts of interest.

Case Report

In May 2011, a 4-year-old girl and her mother returned to the United States after having spent more than 3 weeks visiting family in Uganda, a country where travelers are at high risk for acquiring malaria; neither had taken malaria chemoprophylaxis. While in Uganda, the girl became ill with fever and cough and presented to a clinic for treatment. Diarrhea and vomiting were reported; rash and bleeding were denied and no chronic conditions were reported. The girl was diagnosed with a bacterial infection and given acetaminophen suppositories and unspecified antibiotics. Care for the girl was sought six more times over a 2-week period with continued signs and symptoms. Malaria was reportedly tested for but not diagnosed. High fever was still reported, and the decision was made to return to the United States.

On the return flight to the United States, the girl was very thirsty and drank a large amount of liquid without subsequently urinating either on the plane or in the terminal upon landing. While on a layover at Dulles International Airport (Dulles, VA), she became unresponsive. She was pronounced dead at a hospital an hour later.

Her body was transferred to the Virginia Department of Health Office of the Chief Medical Examiner to perform an autopsy, as required by Virginia law in cases of sudden unexpected death.

On autopsy, she was normally developed and nourished but appeared ill and dehydrated. She had scabbed lesions on the left side of her face and left calf that were consistent with mosquito bites. The internal examination was nonspecific with congestion and edema in various organs and generalized lymphadenopathy. There was no significant trauma, congenital anomaly, or discrete source of infection to cause her death. Elevated urea nitrogen and creatinine consistent with kidney failure were detected in vitreous sample. Tissues, including brain, heart, liver, and kidney, were submitted to CDC for consultation. Histopathology revealed characteristic intra-erythrocyte parasites suggestive of *Plasmodium* species. Immunohistochemistry and polymerase chain reaction assays of autopsy tissues and serum confirmed infection with *Plasmodium falciparum*.

Discussion

Fatal malaria in this child who did not receive chemoprophylaxis or adequate diagnosis and treatment again illustrates the danger of acquiring malaria during travel. Because of the patient's sudden death outside a health care facility, an autopsy was performed and a true cause of death was established. However, other travelers returning from abroad who become ill or expire may be examined without regard to travel status.[5] Death may occur after a latency period,[6] and travel status may not be considered as a part of the cause of death. This might be especially true if the patient was found dead or was too ill to provide details on recent travel. There may be other cases where a true cause of death cannot be established because a postmortem examination was not performed.

To better inform travelers and the clinicians who provide medical advice to persons before and after travel, it is important to understand factors associated with travel-associated severe

illness. Surveillance systems cannot acquire the needed information to better learn from and prevent severe travel-associated illness if the illness is not identified or reported, and illness in patients who die before diagnosis might represent an important gap in our knowledge of these illnesses.

GeoSentinel, a worldwide travel-related illness surveillance system, is one of the largest sources of information about illnesses acquired by travelers. GeoSentinel data reported by Freedman and colleagues identified fewer than 20 deaths between 1996 and 2004.[1] Systematic data are collected at GeoSentinel surveillance sites, often travel medicine clinics,[7] as part of post-travel visits, but the system is unable to capture data on returning travelers who present to an emergency room or primary care provider rather than a travel medicine clinic with severe illness, especially in the United States. Lawson and colleagues reported that based on 3 years of data captured by the Quarantine Activity and Reporting System (QARS), vaccine-preventable and tropical diseases are not major causes of death in international travelers arriving in the United States.[4] Because malaria is not a communicable disease spread person-to-person, reports of malaria are not requested by CDC Quarantine Stations. Only deaths that occurred during travel (on a conveyance or at a US port of entry) are requested. Thus, QARS did not capture 12 malaria deaths associated with international travel reported by the US National Malaria Surveillance System during that same time period.[2] While QARS is capable of collecting travel-related illnesses or deaths, it would not be an effective surveillance system for travel-associated mortality due to malaria.

The cause of death for travelers who died during travel or upon returning from travel might be captured on the US Standard Certificate of Death.[8] However, only the travel-associated data recorded on the death certificate relate to fatal travel-related injury. As a result, data on returning travelers who died as a result of travel-related illness will not be captured systematically by the current version of the US death certificate for inclusion in US vital statistics data. The risks related to travel may not even be considered in assigning cause of death, especially if the signs and symptoms of disease were not overtly suggestive of a specific travel-related illness, such as malaria or rickettsia, whose symptoms may be shared with many other less exotic maladies.

While travel-related information is obtained from ill patients who are able to provide it, the value of a travel history collected by a physician is often limited to its use in diagnosis and treatment. Travel histories collected in a clinical setting for treatment are often not collected at all or are incomplete,[9] which can limit a systematic collection of epidemiologic data related to severe travel-related illnesses. Furthermore, if the patient dies during hospitalization or while seeking treatment, an autopsy may not necessarily be performed, and thus the true cause of death remains a mystery. Autopsy rates in the United States have been steadily declining since the 1970s, with 50% of autopsies now performed on persons whose death was related to an external cause, such as assault, suicide, and accidental poisoning.[10] If a returning traveler (who truly had severe malaria) presented to an emergency department 2 weeks after returning from travel, a diagnosis of renal failure might be made based on creatinine levels. If no clues to the malaria infection were found and that patient subsequently died, his cause of death would be renal failure from unknown etiology. Although a routine autopsy would likely have identified the infection, with rates of hospital-

based autopsy decreasing, the possibility of performing that autopsy is reduced. Additionally, factors such as time of death and autolysis may impair the ability to detect malaria through postmortem microscopy.[11]

Hargarten and colleagues analyzed overseas fatalities in US residents and found that only 1% of overseas deaths were related to infectious disease, with one malaria-related death in the 2-year period of study.[3] More than 5% of deaths analyzed were related to other or unknown causes.[3] This analysis does not take into account deaths occurring in travelers returning home for care, which would likely have increased the number of deaths in the United States.

Surveillance of travel-related infectious diseases should be improved and expanded in ways that allow for capturing of travelers who present late with an illness as a result of infection acquired soon before returning or an extended asymptomatic period. Comprehensive travel status should be considered as part of a standard autopsy investigation.

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